The epidemiology of mumps in Italy

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ARTICLE INFO

Article history:
Received 17 January 2008
Received in revised form 13 March 2008
Accepted 19 March 2008
Available online 8 April 2008

Keywords:
Mumps
Seroprevalence
Vaccination

ABSTRACT

In Italy, although vaccination has been recommended for a number of years, v
mumps is still sub-optimal. The objective of the present study was to evaluat
mumps antibodies in the Italian population, stratified by age, gender and geogra
tion of individuals positive for mumps antibodies remained stable in the age cla
year (25.4% and 30.8%, respectively) and showed a continuous increase after the
percentage of susceptible individuals was higher than 20% in persons 2–14 yea
10% in persons 15–39 years of age. No statistically significant differences were
geographical area. Comparison between these results and the data obtained fron
a statistically significant increase in seroprevalence in the age class 2–4 years. No
in the other age-groups. The results of this study confirm that the efforts made in
vaccination coverage within the second year of life should be strengthened.

1. Introduction

Mumps is an acute contagious disease which is endemic worldwide [1]. Infection typically occurs in childhood, though it can also occur in adults, among whom some complications can be more frequent than among children. Infection, even if asymptomatic, induces a long-lasting immunity [2].

The disease is usually benign, and 30% of paediatric cases are asymptomatic. Severe complications, though rare, include hearing loss in children (5/100,000) and encephalitis (incidence of <2/100,000 cases, of which 1% are fatal). Adults have a greater risk than children of meningo-encephalitis. When acquired after puberty, mumps can be related to orchitis, testicular atrophy and even sterility in males, and to mastitis and oophoritis in females. Mumps infection in the first 12 weeks of pregnancy may result in foetal loss [3]. Other important characteristics of mumps are the occurrence of asymptomatic forms, preceding the possible clinical onset, and therapy.

The epidemiological impact of mumps ar
lae have prompted the development of a vac
represents the best option for preventing the
plications.

The mumps vaccine contains live attenua
able as a single-antigen preparation, as a trival
measles and rubella vaccines (MMR) [4], or as
nation with measles, rubella and varicella va
10 different live attenuated viral strains are
vaccines worldwide.

In Italy, for many years the Rubini strain h
The poor effectiveness in preventing mumps
nationwide use has contributed to the failure
ease in the 1990s [6]. In June 2001 the regist
containing this specific vaccine strain was r
then widely used live attenuated mumps va
have included or include the Jeryl Lynn, Urab

The adoption of a single dose schedule
cant decrease in the incidence of mumps, ye
to occur in school settings [8–10]. A two-dos
edly even more effective in decreasing mum
allowed many countries to achieve near-el

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0264-410X/$ – see front matter
doi:10.1016/j.vaccine.2008.03.040

ology of mumps in Italy using a number of data sources and to determine whether or not there have been changes in seroprevalence by comparing the results of two studies conducted 8 years apart.

2. Materials and methods

2.1. Incidence data

In Italy, mumps is subject to mandatory notification [18], and all reported cases are recorded by Italy's National Census Bureau (ISTAT). The clinical case definition is sufficient for a case to be reported; laboratory diagnosis is not required. The clinical case definition is a mono or bi-lateral swelling of salivary glands (parotidis or others glands) lasting at least 2 days and absent/moderate fever, without other concomitant pathologies.

We calculated the incidence for the period 1991–2004 for the entire country and for three main geographical areas (northern Italy, central Italy, and southern Italy and the islands), based on mandatory notifications, using as reference the Italian population included in the national census (for the years 1991 and 2001) or estimates provided by ISTAT (for the remaining years). We also calculated the trend in incidence for the periods 1991–1995, 1996–2000 and 2001–2004, by age class: 0–14, 15–24, 25–64, and $\geq$65 years. For each of these periods, the trend in incidence by geographical area and the percentage of notifications in different age groups were also determined.

2.2. Analysis of other databases

Given that mandatory notification is affected by underreporting, we analysed data from other databases with information on mumps. In particular, we considered the incidence data for the years 2000–2004 provided by Italy's Paediatric Sentinel Surveillance System of Vaccine-Preventable Diseases (SPES), a network of paediatricians located throughout Italy and co-ordinated by the Istituto Superiore di Sanità (Italy's National Health Institute). We also examined the National Hospital Discharge Database, created in 1994, which collects information on all hospitalisations recorded in Italy [19]. For the analysis of this latter database, we considered the main reason for hospitalization, which is codified using the ICD9-CM code (0072 for mumps). The analysis was performed on data for the period 1999–2004.

2.3. Seroprevalence study

A national cross-sectional population-based seroprevalence study of mumps antibodies was performed on samples collected in the period from January 2003 to October 2004 in each of Italy's 19 Regions and 2 Autonomous Provinces. Assuming an overall mumps prevalence of 70%, a sample size of 2017 sera was required to

equally representative of males and fem
were quantified using an immunoenzyme
nost Anti-Parotitis-Virus IgG, Dade Behrin
high sensitivity and specificity (95.4% and 9

The following criteria were applied fo
tion:

IgG negative sample
IgG positive sample
Equivocal IgG sample

The equivocal samples were retested
firmed, the sample was classified as "equ
samples were quantitatively evaluated usin
Log_{10} titer = $\alpha \times \Delta E^{\beta}$, where α and β repre
stants. Antibody activity was expressed as

2.4. Statistical analysis

The statistical analysis was performed
Macintosh (Abacus Concepts, Inc., Berkele
lence data were summarized as percentage
titres were presented as geometric mean
percentages were assessed by the χ^2-te
between geometric mean titres were asses
logarithmically transformed values. The da
gender and geographical area and were the
obtained from a seroprevalence study con
same assay and cut-off [21].

3. Results

3.1. Incidence data

Based on data provided by ISTAT, mu
affect a large portion of the population an
an endemo-epidemic course, with outbrea
overall annual incidence ranged from 125.1
population in the years 1991–2004 (Fig. 1)

For all three periods (1991–1995, 1996
and the different age groups (0–14, 15–24,
was clear that mumps mainly affects chil
ever, in this age group, the incidence progre
decreased ($p < 0.01$), from 409.2 cases pe
1991–1995, to 365.9 in 1996–2000 to 97.6
trend, with a significantly decreasing inci
other age groups when comparing differen
for persons older than 65 years of age whe
to 2001–2004, $p < 0.05$).

When comparing persons 0–14 years o
uals, the differences in the percentage of ca
change over the three periods. The analys
showed that the trend in incidence was s

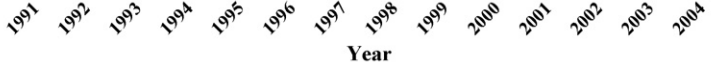

Figure 1. Annual mumps incidence per 100,000 population in Italy between 1991 and 2004 (total and by geographic areas) (Italy's National

Table 1
Incidence of mumps per 100,000 children 0–14 years, Italy, 2000–2004

Year	Northern (Italy)	Central (Italy)	Southern (Italy)	Italy
2000	1917	2274	1830	1939
2001	1518	665	761	1039
2002	302	206	150	220
2003	215	81	116	149
2004	109	65	54	79

Data from paediatric sentinel surveillance (SPES).

the three areas and that there was a clear north–south gradient, with the highest incidence consistently found for northern Italy, followed by central and southern Italy (Fig. 1).

3.2. Analysis of other databases

In the period 2000–2004, 11,697 cases of mumps were reported to SPES, with the annual incidence progressively decreasing from 1939 per 100,000 children (0–14 years) (2000) to 79 per 100,000 children (2004). In general, incidence rates were higher in northern and central Italy than in southern Italy (Table 1).

According to the National Hospital Discharge Database, in the period 1999–2004 there was an annual mean of 363 hospitaliza-

tions and 247-day-hospital admissions for m
2000 (619 and 325 hospitalizations and day
respectively). The mean duration of stay was

3.3. Seroprevalence study

Overall, 3094 blood samples were analyse
621 were negative, and 197 were equivoca
showed a typical pattern. In the first year o
are passively protected by the mother), 25.4
months old were seropositive; among 12–23-
prevalence was 30.8% (difference not significa
the seroprevalence significantly increased
pared to 12–23-month olds); it continued
though not always significantly: 65.0%, 78.
92.8%, respectively, for the age classes 5–9,
and >40 years (Fig. 2). Of note was the findin
of seronegative individuals was greater than
2–4, 5–9 and 10–14 years and greater than
15–19 and 20–39 years.

No statistically significant difference was
lence when comparing males and females
seroprevalence was basically uniform when
geographic areas, with no significant differen

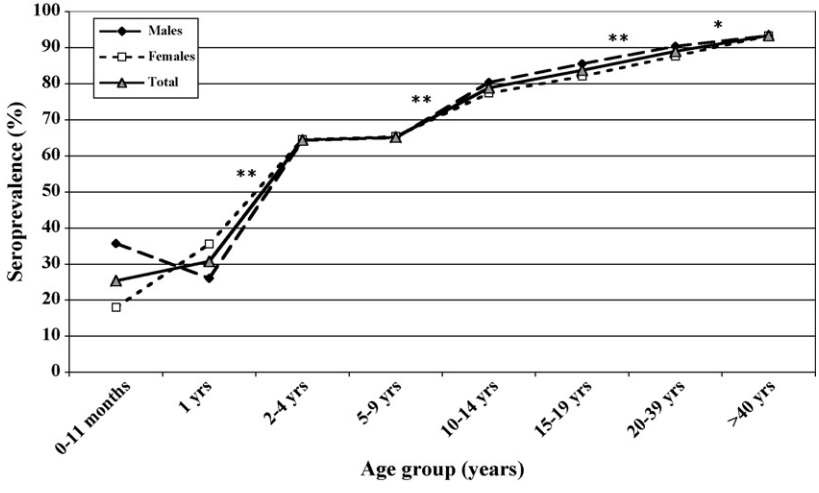

Figure 2. Mumps seroprevalence by age group and gender in Italy (2004). χ^2-test: $^*p < 0.05$; $^{**}p < 0.01$.

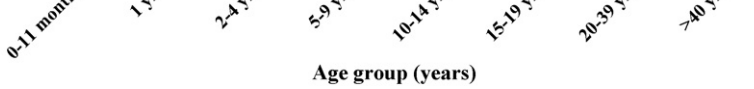

Figure 3. Mumps seroprevalence by geographical area in Italy (2004).

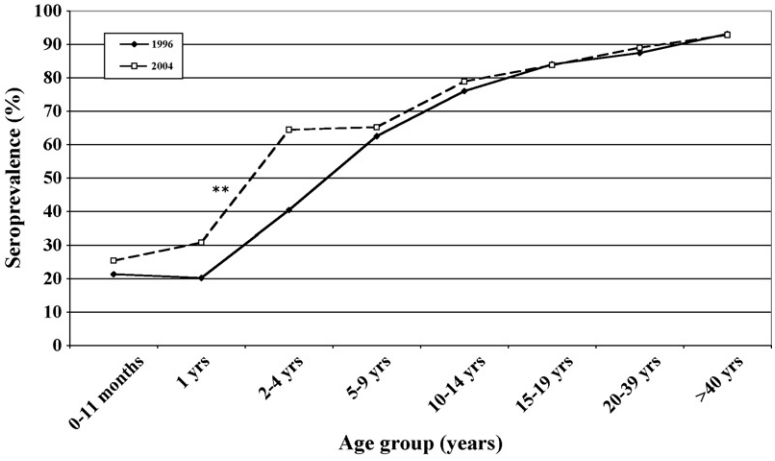

Figure 4. Comparison between mumps seroprevalence by age-group, Italy 1996 and 2004. χ^2-test: $^{**}p < 0.01$.

The GMT progressively increased up to 10–14 years and then significantly ($p < 0.01$) decreased in the age class 15–19 years. There were no significant differences when comparing males and females, except for the age group 15–19 years ($p < 0.01$).

3.4. Comparison of seroprevalence data from 1996 and 2004

Only in the age group 2–4 years was the seroprevalence in the survey conducted in 2004 statistically higher than that in 1996 ($p < 0.01$). No significant differences were detected in other age classes (Fig. 4).

4. Discussion

Before vaccination was introduced, mumps was a common infectious disease in all parts of the world, with the highest annual incidence among 5–9-year olds. In many countries, the availability of safe and efficacious vaccines has led to a rapid decrease in morbidity. According to WHO, in 2004, mumps vaccination was included in the vaccine schedules of 109 countries, which constitutes a marked increase with respect to the 74 countries in 1999. In 2004, a two-dose vaccination schedule, mainly with the MMR vaccine, was extensively adopted (in 82% of the 109 countries) [22].

In countries where it was possible to im
to rapidly achieve and maintain high VC, th
decrease in morbidity [3].

In Italy, mumps vaccination was intro
of 1980s and in 1982 the Ministry of He
cination of susceptible males, both in pre
availability of combined MMR vaccines
immunization of both males and females i
and MMR vaccination has been included
schedule since the beginning of 1990s. A
commercially available contained at lea
of the following mumps strains: Jeryl L
The impact of vaccination on mumps wa
tions changed from 62,000 per year in
to 45,000 in the period 1990–1997. Epid
tered every 3–4 years and over 80% of
up to 15 years of age. During 1990s the
cases in already vaccinated subjects prom
studies on the efficacy of commercially
result was that the Rubini strain had a
(23–31%) and that its wide use could be r
tory control of mumps at national level [23
in July 2001 products containing Rubini
[7].

(from 85.7% in 2004 to 87.3% in 2005), as a result of the activities required by the national plan for the elimination of measles and congenital rubella through vaccination with the combined MMR vaccine [28].

However, VC is still not sufficient because the control and/or elimination/eradication of an infectious disease can only be achieved by reaching and maintaining a 95% VC [4], so as to avoid undesired effects, such as new cohorts of susceptible individuals, an increase in the mean age of acquisition of the infection, and the broadening of the inter-epidemic period. The commitment made by Italy to eliminate measles and congenital rubella (<1 case/100,000 newborns) by 2010 [29] will also allow Italy to reach the targets established for mumps for the WHO European Region, which have been endorsed in the 2003–2005 National Health Plan and the 2005–2007 National Vaccine Plan [15,30,31].

In Italy, mumps incidence remained almost unchanged until 2001 (range: 25.9–125.1/100,000 inhabitants) and outbreaks were reported every 2–4 years. Since 2002, notifications have rapidly decreased, and in 2004 the lowest number of cases (2,604) was reported (incidence of 4.5/100,000 inhabitants). In the same period, data collected by the Istituto Superiore di Sanità through the SPES sentinel network confirmed this trend yet highlighted that the routine notification system suffers from remarkable underreporting. Concerning this last point, it should be stressed the need for a better case definition for surveillance as mumps symptoms can be easily misinterpreted if not associated to an outbreak. Noteworthy, when the incidence of mumps decreases, laboratory confirmation should be necessary. Nonetheless, recent epidemiological data show a decrease in mumps cases yet not an increase in the mean age of acquisition of infection, as already reported in other countries [32–35].

Comparison of seroprevalence data from 1996 and 2004 showed a statistically significant increase in seroprevalence only in the age class 2–4 years (41.2% vs. 64.4% in 1996 and 2004, respectively) [21]. This seems to be the result of the latest immunization campaigns; the efforts recently sustained in order to address the national plan for the elimination of measles and congenital rubella through vaccination have had a significant impact on seroprevalence data.

Of note is the finding that in this age class, as well as in the 5–9- and 10–14-year age classes, more than 20% of children were seronegative, and more than 10% of individuals 15–39 years of age were susceptible.

These results demonstrate that VC in Italy is still sub-optimal and that there exists a risk of outbreaks. The lack of adequate vaccine data processing management in some Regions and the high rate of parents (18%) who intend to vaccinate their children at an older age [17] could explain these observations and represent a critical point in planning further priority activities.

In conclusion, this research highlights that vaccination strategies and programmes should be further strengthened if the targets

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